12/14/84 BB-1025
TXR-4170

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY 004170
WASHINGTON, D.C. 20460

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

Caswell No: 586
EPA Chem. No: 034401

SUBJECT: NALED RS - Company data submitted under Acc. #253453 (Tox Data) - 10 reports and Acc. #253454 (Purity of SX-1240 = 93.0%, and SX-1397 - 91.5%) Reg. #2339-1633 and 239-2297.

TO: William Miller, PM 16
Registration Division (TS-767C)

FROM: Irving Mauer, Geneticist
Section VI, Toxicology Branch
Hazard Evaluation Division (TS-769) 12-13-84

THRU: Jane E. Harris, Ph.D. Jane E. Harris 12-14-84
Section Head, Sections VI
Toxicology Branch/HED (TS-769C)

and

Theodore Farber, Ph.D., Chief
Toxicology Branch/HED (TS-769C)

The following company tox. data (10 reports) have been submitted by Chevron under cover letter of June 1, 1984:

Chevron Naled Technical
EPA Reg. No. 239-1633
158.135 Toxicology

Table of Contents

Title of Study

1. The Efficacy of Atropine Sulfate and Pralidoxime Chloride (2-PAM) as Antidotes for the Acute Oral Toxicity of Naled Technical in Rats. SOCAL No. 2036. 12/10/82 S-1781

004170

2. The Efficacy of Atropine Sulfate and Pralidoxime Chloride (2-PAM) as Antidotes for the Acute Oral Toxicity of DIBROM Technical. SOCAL No. 1679. 12/21/81 S-1781

3. Effect of Vehicle on the Acute Oral Toxicity of Naled Technical (SX-1397) in Adult Male and Female Rats. SOCAL No. 2105. 2/9/84

4. Addendum to Acute Oral Toxicity Study in Rats with Naled Technical (SX-1397) in Corn Oil and Aqueous Suspensions. SOCAL Project No. 2105. Dosage Formulations Analyses. J. Slagowski et al. Chevron Chemical Co. 11/18/83

5. Addendum to Teratology Study in Rats with Naled Technical (SX-1397). Science Applications Inc. Project No. 583008. Chevron No. S-2276. Dosage Formulation Analyses. 8/30/83

6. Moriya, M. et al. Further Mutagenicity Studies on Pesticides in Bacterial Reversion Systems - Mutation Research. 116 185-216 (1983)

7. Braun, R. et al. Activity of Organophosphorus Insecticides in Bacterial Tests for Mutagenicity and DNA Repair - Direct Alkylation Versus Metabolic Activation and Breakdown. II. 0,0-Dimethyl-0-(1,2-dibromo-2,2-dichloroethyl)-phosphate and two O-Ether Derivatives of Trichlorfon. Chem. Biol. Interaction 43:361-380 (1980)

8. Hanna, P.J., and Dyer, K.F. Mutagenicity of Organophosphorus Compounds in Bacteria and Drosophila. Mutation Research 28:405-420 (1975)

9. Byeon, W.H., et al. Salmonella/Microsomal Enzyme Activation System. Mutagenicity of Pesticides in the Salmonella/Microsome System. Korean J. Microbiol. 14:128-134 (1976)

10. In Vivo Cytogenetics Study in Rats. Naled Technical (SX-1397), EG&G Mason Research Institute MRI-193-CCC-82-82. 6/6/83. S-2167

The following data gaps for technical naled have been identified in the Registration Standard (dated 12/22/82, as amended 6/23/83, page 8):

Acute inhalation in the rat (NOEL)
Subchronic inhalation (NOEL)
21-Day dermal
Two-year oral in the rat
One-year oral in the dog

Naled

Page __3___ is not included in this copy.

Pages _____ through _____ are not included in this copy.

The material not included contains the following type of information:

_____ Identity of product inert ingredients.

_____ Identity of product inert impurities.

_____ Description of the product manufacturing process.

_____ Description of product quality control procedures.

_____ Identity of the source of product ingredients.

_____ Sales or other commercial/financial information.

_____ A draft product label.

_____ The product confidential statement of formula.

_____ Information about a pending registration action

_____ FIFRA registration data.

_____ The document is a duplicate of page(s) _____

__X__ The document is not responsive to the request.

Information is internal deliberative.

The information not included is generally considered confidential by product registrants. If you have any questions, please contact the individual who prepared the response to your request.

004170

Two-generaiton reproduction in the rat
Teratology in the rat
Teratology in the rabbit
Metabolism in one species (rat, or dog)
Mutagenicity: Gene mutation in mammalian cells
: Chromosomes aberrations in mammalian systems
: DNA damage/repair in mammalian systems

TB CONCLUSIONS

Although Studies 1 and 2 (antidotal assays), as well as 3 and 4 (vehicle/acute LD-50 validation studies), do not contribute any information needed to fulfill regulatory requirements for this chemical, they have been evaluated here (see attached DATA REVIEWS). Study 5 has already been reviewed by Toxicology Branch under Accession #252451 (Memo, May 22, 1984: Mauer to Miller) and adjudged CORE MINIMUM Data. Studies 6 and 7 are published bacterial mutagenicity review/survey articles, but the Moriya paper is deficient in specific experimental details. Studies 8 and 9 (also published articles) have already been reviewed for the NALED REGISTRATION STANDARD, and judged UNACCEPTABLE. Only Chevron Report No. 10 above is directly responsive to the data required for the continued registration of pesticidal products containing naled-technical. The Agency, however, is satisfied with the data already received for bacterial mutagenicity testing (Naled PRS, June 1983, Table A).

In Summary, the following are the assessments on the adequacy of the tox. studies submitted under ACCESSION NO. 253453, and not previously evaluated by TB (see attached DATA REVIEWS to this memo):

Study No.	TB EVALUATION/CORE
1	ACCEPTABLE
2	ACCEPTABLE
3	ACCEPTABLE
4	ACCEPTABLE
5	CORE MINIMUM
6	UNACCEPTABLE
7	ACCEPTABLE
8	UNACCEPTABLE
9	UNACCEPTABLE
10	UNACCEPTABLE

Attachment

#1 - OK J Meaver 12-5-83

004170

TOXICOLOGY BRANCH: DATA REVIEW

CHEMICAL: NALED Casewell: 586

STUDY TYPE: Antidotal - rat EPA Chemical #: 034401

CITATION: The Efficacy of Atropine Sulfate and Pralidoxime Chloride (2-PAM) as Antidotes for the Acute Oral Toxicity of Naled Technical in Rats.

ACCESSION No./MRID No.: 253453/NA

SPONSOR/TESTING LAB.: Chevron/Chevron Environmental Health and Toxicology Lab., Richmond, CA

STUDY No./DATE: Socal #2036/December 30, 1982

TEST MATERIAL: SX-1397, Naled Technical, 92.6% a.i., a clear colorless liquid.

PROCEDURES: The attached M & M appear to be adequate to generate valid results. A GLP/QA statement dated February 7, 1983, from Schollar Associates, Novato, CA, accompanied this study.

RESULTS: Compared to oral LD_{50}'s of 371 (275-500) mg/kg in adult S-D derived males and 207 (154-278) mg/kg in females given naled alone, post-treatment administration of atropine sulfate or a combination of pralidoxime chloride plus atropine resulted in male/female LD_{50}'s of 533 (332-855) mg/kg/376 (273-517) mg/kg and 479 (341-674) mg/kg/400 (249-040) mg/kg, respectively, i.e., increases of 1.3 to 1.9 times greater. Time-to-death and survivor-recovery-times for animals receiving the antidotes increased by 1 to 2 days over those given naled alone. Tremors and salivation observed in naled-treated animals receiving no antidote virtually disappeared in naled plus antidotal groups, whereas fasciculations were reported one to three hours longer in naled antidotal-treated animals compared to the 10 minute to 1 hour 15 minutes in animals receiving only naled alone. The incidences of other signs of OP toxicity were reported to be similar in all groups and no significant differences among control and treated groups were recorded in body weights. No gross pathological lesions attributable to test material were reported at necropsy.

CONCLUSIONS: Post-naled (oral) treatments with atropine or a combination of atropine plus 2-PAM (both i.m.) were protective in adult rats.

TB EVALUATION: Acceptable.

A comprehensive protocol according to FIFRA Guidelines, however, should have included atropinized animals treated with naled.

(1) LC-92

0041

Environmental Health Toxicology

Chevron

THE EFFICACY OF ATROPINE SULFATE AND PRALIDOXIME CHLORIDE (2-PAM) AS ANTIDOTES FOR THE ACUTE ORAL TOXICITY OF NALED TECHNICAL IN RATS

SOCAL 2036

DECEMBER 30, 1982

Submitted By: C E Duke 1/7/83
C. E. Duke
Toxicology Technician

Reviewed By: J R Cushman 1/7/83
J. R. Cushman, Ph.D.
Experimental Toxicologist

Approved By: Z. A. Wong 2-3-83
Z. A. Wong, Ph.D.
Supervising Toxicologist

7

Chevron Environmental Health Center, P.O. Box 1272, Castro and Midway Streets, Richmond, California 94802

Chevron Environmental Health Center, P.O. Box 1272, Castro and Midway Streets, Richmond, California 94802

Naled

Page _____ is not included in this copy.

Pages __8__ through __9__ are not included in this copy.

The material not included contains the following type of information:

_____ Identity of product inert ingredients.

_____ Identity of product inert impurities.

_____ Description of the product manufacturing process.

_____ Description of product quality control procedures.

_____ Identity of the source of product ingredients.

_____ Sales or other commercial/financial information.

_____ A draft product label.

_____ The product confidential statement of formula.

_____ Information about a pending registration action

__X__ FIFRA registration data.

_____ The document is a duplicate of page(s) _____

_____ The document is not responsive to the request.

The information not included is generally considered confidential by product registrants. If you have any questions, please contact the individual who prepared the response to your request.

2 - 014 - J. Stewart 12-5-84

004170

TOXICOLOGY BRANCH: DATA REVIEW

CHEMICAL: NALED Casewell: 586

STUDY TYPE: Antidotal - rat EPA Chemical #: 034401

CITATION: The Efficacy of Atropine Sulfate and Pralidoxime Chloride (2-PAM) as Antidotes for the Acute Oral Toxicity of DIBROM Technical.

ACCESSION No./MRID No.: 253453/NA

SPONSOR/TESTING LAB.: Chevron/Chevron Environmental Health and Toxicology Lab., Richmond, CA

STUDY No./DATE: Socal #1679/December 21, 1981

TEST MATERIAL: SX-1240, Dibrom technical, 93.0% a.i., a pale, yellow liquid.

PROCEDURES: The attached M & M appear to be adequate to generate valid results. A GLP/QA statement dated February 8, 1982, from Schollar Associates, Novato, CA, accompanied this study.

RESULTS: Compared to oral LD_{50}'s of 386 (271-549) mg/kg for adult S-D derived males and 236 (167-334) mg/kg for females given Dibrom technical alone, post-treatment injection of atropine sulfate or 2-PAM resulted in male/female LD_{50}'s of 487 (339-702) mg/kg/386 (271-549) mg/kg and 414 (286-600) mg/kg/263 (168-413) mg/kg, respectively, i.e., increases of 1.1 to 1.6 times greater. Time-to-death and time-of-recovery were apparently not affected by antidotal treatment, and no significant differences between groups were recorded in body weights. Signs of toxicity (tremors, salivation, motor activity, g.i. distress, fasciculations, etc.,) were less severe in both antidotal groups. At necropsy, no gross pathological changes attributable to test material were reported.

CONCLUSIONS: Post-naled (oral) treatment with atropine or 2-PAM (i.m.) protected adult rats against severe naled generated toxicities but, except for females given additional atropine (LD_{50} 1.6 x naled alone), apparently not against lethal consequences of acute naled treatment.

004170

TB EVALUATION: Acceptable.

A comprehensive protocol according to FIFRA Guidelines, however, should have included antropinized animals treated with naled.

Standard Oil Company of California

(2)

Environmental Health Toxicology

Dibrom S-1781 004170
EC-77

Chevron

THE EFFICACY OF ATROPINE SULFATE AND PRALIDOXIME CHLORIDE (2-PAM) AS ANTIDOTES FOR THE ACUTE ORAL TOXICITY OF DIBROM TECHNICAL IN RATS

SOCAL 1679

DECEMBER 21, 1981

Submitted By: C. E. Duke 1-25-82
C. E. Duke
Toxicology Technician

Reviewed By: C. M. Cisson 1-27-82
C. M. Cisson, Ph.D.
Experimental Toxicologist

Approved By: Z. A. Wong 2-3-82
Z. A. Wong, Ph.D.
Supervising Toxicologist

Naled

Page _____ is not included in this copy.

Pages 13 through 15 are not included in this copy.

The material not included contains the following type of information:

_____ Identity of product inert ingredients.

_____ Identity of product inert impurities.

_____ Description of the product manufacturing process.

_____ Description of product quality control procedures.

_____ Identity of the source of product ingredients.

_____ Sales or other commercial/financial information.

_____ A draft product label.

_____ The product confidential statement of formula.

_____ Information about a pending registration action

__X__ FIFRA registration data.

_____ The document is a duplicate of page(s) _____

_____ The document is not responsive to the request.

The information not included is generally considered confidential by product registrants. If you have any questions, please contact the individual who prepared the response to your request.

TOXICOLOGY BRANCH: DATA REVIEW

Chemical: Naled

Caswell: 586
Study Type: Acute Oral LD_{50} - rat EPA Chem.# 034401

Citation: Effect of Vehicle on the Acute Oral Toxicity of Naled Technical (SX-1397) in Adult Male and Female Rats.

Accession No./MRID No.: 253453/NA

Sponsor/Testing Lab.: Chevron/Chevron Environmental Health & Toxicology Lab., Richmond, CA

Study No./Date: Socal No. 2105/February 9, 1984.

Test Material: Naled Technical, SX-1397, 92.6% ai, a pale-yellow liquid

Procedures: The attached M & M appear to be adequate to generate valid results. A GLP/QA statement, dated March 29, 1984, from Schollar Associates (Novato, CA) is included in this study.

Results: The following LD_{50}'s were reported with the two vehicles:

Vehicle	Sex	LD50 (95% CL)	Slope (95% CL)
Corn Oil	Male	325 (167-633) mg/kg	1.6 (0.7-3.8)
	Female	230 (96-550) mg/kg	1.6 (0.6-4.1)
0.5% CMC	Male	191 (113-325) mg/kg	2.0 (1.0-3.9)
	Female	92 (54-159) mg/kg	2.0 (1.0-3.7)

Corn oil values were reported to be comparable to previous studies with this vehicle conducted with other technicals (SX-1397, SX-1240). Except for increased diarrhea with corn oil, typical OP toxicity was observed with both vehicles in comparable incidences. The authors suggested the higher LD_{50} values found with corn oil may be due in part to "an increased rate of movement of the corn oil preparation throughout the digestive tract as indicated by the increase of diarrhea," an explanation with which this reviewer concurs. No significant differences from control or between vehicles in mean body weights nor in pathology were recorded.

Conclusions: Naled Technical dissolved in corn oil was less lethal than the same chemical suspended in CMC, as reflected in higher oral LD_{50} values for both treated male and female rats.

TB Evaluation: Acceptable.

(3)

004170

Environmental Health & Toxicology

2119

Chevron

EFFECT OF VEHICLE ON THE ACUTE ORAL TOXICITY

OF

NALED TECHNICAL (SX-1397) IN ADULT MALE AND FEMALE RATS

SOCAL 2105

February 9, 1984

Submitted By: D. A. Cerkanowicz / JRC 3-21-84
D. A. Cerkanowicz
Toxicology Technician

Reviewed By: J. R. Cushman 3-21-84
J. R. Cushman, Ph.D.
Experimental Toxicologist/Study Director

J. M. Holland 3-22-84
J. M. Holland, DVM, Ph.D.
Chief of Pathology

Approved By: Z. A. Wong 3-24-84
Z. A. Wong, Ph.D.
Supervising Toxicologist

Naled

Page _____ is not included in this copy.

Pages 19 through 21 are not included in this copy.

The material not included contains the following type of information:

_____ Identity of product inert ingredients.

_____ Identity of product inert impurities.

_____ Description of the product manufacturing process.

_____ Description of product quality control procedures.

_____ Identity of the source of product ingredients.

_____ Sales or other commercial/financial information.

_____ A draft product label.

_____ The product confidential statement of formula.

_____ Information about a pending registration action

__X__ FIFRA registration data.

_____ The document is a duplicate of page(s) _____

_____ The document is not responsive to the request.

The information not included is generally considered confidential by product registrants. If you have any questions, please contact the individual who prepared the response to your request.

#4-OK Glaven 12-3-84 004170

TOXICOLOGY BRANCH: DATA REVIEW

Chemical: Naled

Caswell: 586
EPA Chem.# 034401

Study Type: Dosage Formulation Analyses

Citation: Addendum to Acute Oral Toxicity Study in Rats with Naled Technical (SX-1397) in Corn Oil and Aqueous Suspensions. SOCAL Project No. 2105. Dosage Formulations Analyses.

Accession No./MRID No.: 253453/na

Sponsor/Testing Lab.: Chevron/Ortho Agricultural Division, Richmond, CA

Study No./Date: Socal #2105/ 11-18-83

Test Material: Naled technical, SX-1397, 92.5% ai

Procedures: The M & M appended here appear to be adequate.

Results: Analytical data were provided in this report for corn oil dose-level preparations from the dosing period between 95% and 104% of nominal, and for the CMC preparations, 93.7% and 104%.

Conclusions: The data appear to demonstrate that the actual dosage levels were within acceptable limits of nominal (as derived from preliminary mixing).

TB Evaluation/CORE: Acceptable

(4)

721 11
Dithro...
004170

CHEVRON CHEMICAL COMPANY
ORTHO AGRICULTURAL CHEMICALS DIVISION
RESEARCH AND DEVELOPMENT DEPARTMENT
RICHMOND, CALIFORNIA

TITLE: ADDENDUM TO ACUTE ORAL TOXICITY STUDY IN RATS WITH NALED TECHNICAL (SX-1397) IN CORN OIL AND AQUEOUS SUSPENSIONS
SOCAL PROJECT NO. 2105
DOSAGE FORMULATION ANALYSES.

DATE: November 18, 1983

CHEVRON FILE NO: 721.11/SOCAL 2105

PURPOSE: To provide analytical data on dosage formulations in support of an acute oral toxicity study in rats.

Date Study Initiated: June 27, 1983

Date Study Completed: July 22, 1983

Principal Investigator: J. L. Slagowski — 12-8-83 Date

Supervisor: J. B. Leary — 12/8/83 Date

Study Authorized By: J. Abell — 12/8/83 Date

Study Audited By: Quality Assurance Unit — 12/8/83 Date

Distribution List:

J. R. Cushman
J.K. Kodama
L.R. Stelzer
R. A. Zimmerman
R&M Files
R&D Files

Naled

Page _____ is not included in this copy.

Pages _24_ through _26_ are not included in this copy.

The material not included contains the following type of information:

_____ Identity of product inert ingredients.

_____ Identity of product inert impurities.

_____ Description of the product manufacturing process.

_____ Description of product quality control procedures.

_____ Identity of the source of product ingredients.

_____ Sales or other commercial/financial information.

_____ A draft product label.

_____ The product confidential statement of formula.

_____ Information about a pending registration action

__X__ FIFRA registration data.

_____ The document is a duplicate of page(s) _____

_____ The document is not responsive to the request.

The information not included is generally considered confidential by product registrants. If you have any questions, please contact the individual who prepared the response to your request.

00410

Chemical: Naled

Caswell: 586
EPA Chem.# 034401

Study Type: Mutagenicity: Gene mutation by bacterial reversion.

Citation: Moriya, M. et al. Further Mutagenicity Studies on Pesticides in Bacterial Reversion Systems. Mutation Research 116:185-216 (1983)

Accession No./MRID No.: 253453/na

Sponsor/Testing Lab.: (Published article)

Study No./Date: n/a

Test Material: Sample reportedly obtained from the Agricultural Chemicals Inspection Station of the (Japanese) Ministry of Agriculture, Forestry and Fisheries at Kodaira; purity and solubility not provided.

Procedures: Specific procedures for naled were not detailed in this published review article. Naled was among 228 pesticides presumably tested for mutagenicity in the Salmonella/Microsome (Ames) Assay and with the WP2-hcr strain of Escherichia coli.

Results: No specific data or results were provided in this review for naled.

Conclusions: Inconclusive due to lack of data on test chemical.

TB Evaluation/Core: Unacceptable

ATTACHMENT 1

TOXICOLOGY BRANCH: DATA REVIEW

Caswell No: 586
Chemical: Naled EPA Chem. No: 034401

Study Type: Mutagenicity: Gene mutation and DNA-damage/repair in bacteria.

Citation: Braun, R. et al. Activity of Organophosphorus Insecticides in Bacterial Tests for Mutagenicity and DNA repair - Direct Alkylation Versus Metabolic Activation and Breakdown. II. 0,0-Dimethyl-0-(1,2,-dibromo-2,2-dichloroethyl)-phosphate and two O-Ether Derivatives of Trichlorfon. Chem. Biol. Interaction 43:361-380 (1980)

Accession No./MRID No.: 253453/na

Sponsor/Testing Lab.: (Published article)

Study No./Date: N/A

Test Material: Reportedly synthesized from dichlorovos and provided by Dr. W. Georgi of the VEB Fettschemie Karl-Marx-Stadt, GDR; purity not provided in this paper.

Procedures: Naled was among three OP's tested for DNA damage (differential toxicity) in Proteus mirabilis strains PG273 (wild-type) and PG 713 (thr- rec- hcr-), and for gene mutation (by reversion to prototrophy) in the his- strain TA 100 of Salmonella typhimurium), both in the absence and presence of mouse liver S-9 postmitochondrial supernatant fractions (for mammalian metabolic activation), Aroclor-1254 stimulated (= MA).

Results: DNA-damage tests in P. mirabilis were negative (equally toxic to both strains) at inhibitory concentrations of 10 and 40 uM/plate, but positive for reversion in TA 100 in plate incorporation tests at the mid-dose, 1.0 uM/plate of three levels tested both with/without MA. The HDT, 2.0 uM, was toxic in the absence of MA, but mutagenic in its presence, whereas the LDT, 0.5 uM, was only marginally positive (<2-fold compared to DMSO controls). The authors state that Naled was not mutagenic in strain TA 1535 or in frame-shift mutation detecting strains, although the data were not presented.

Conclusions: Naled was a direct mutagen (active in the absence of MA) in Salmonella TA 100, and its metabolites presumably provide slightly more potent mutagenicity in the presence of a mouse metabolic system provided by PCB-stimulated hepatic microsomes.

TB Evaluation: Acceptable

U 12-1-
004170

Chemical: Naled

Caswell No.: 586
EPA Chem. No.: 034401

Study Type: Mutagenicity: in vivo cytogenetics in rats.

Citation: In Vivo Cytogenetics Study in Rats: Naled Technical (SX-1397)

Accession No./MRID No.: 253453/NA

Sponsor/Testing Lab.: Chevron Chemical (Ortho), Richmond, CA/ EG&G Mason Research, Worcester, MA

Study No./Date: MRI-193-CCC-82-82/June 16, 1983

Test Material: Naled technical (SX-1397), a straw-colored liquid (purity not stated by contract lab.) administered in carboxymethyl-cellulose (CMC).

Procedures: As given in the attachment to this review (MRI protocol 11.136), with six (6) Protocol Amendments which did not affect either the conduct of the study, nor the validity of the results generated. A quality Assurance Statement was included in the final report, to assure compliance with GLP's.

Results: Based upon oral LD_{50}'s of 85.1 mg/kg (70.7-102.2 mg/kg) for Charles River male Sprague-Dawley rats (MTD = 38.87 mg/kg), and 81.2 mg/kg (72.5-91.0 mg/kg) for females (MTD = 61.7 mg/kg), both generated by MRI, the following results (this memo) were reported in this oral cytogenetic study, performed according to standard protocols for this type of assay. Three control groups were run at this same time: A negative control with distilled water; a solvent control (CMC); and a positive control, cyclophosphamide (CP).

Conclusions: From the results reported the authors conclude that, "... it would appear that SX-1397 had no clastogenic effect when the test groups are compared to the vehicle control group treated with carboxymethyl cellulose...." in either sex, in contrast to the positive result (significant increase in aberrations) in bone-marrow cells from CP-treated animals. Neither modal chromosome numbers nor mitotic indices were apparently altered by naled treatment (Tables 8 to 18), which indicates to this reviewer that an "effective" (i.e., cytotoxic) dose was not delivered to the target tissue from the oral route of administration, i.e., insufficient dosage was administered, especially to males.

TB Evaluation: Not acceptable, because in males, no evidence of absorption of a non-toxic dose from the g.i. tract was presented, and in both males and females, no evidence that an effective concentration of active chemical (to effect cytotoxicity) was reached at the target tissue (bone marrow cells).

Oral Dose (mg/kg, once)		No. of Animals				No. of Metaphases*** Examined		Mean Chromosome Aberrations in Group****					
		Died		Toxicity**				6-Hours		24-Hours		48-Hours	
Males*	Females*	M	F	M	F	Males	Females	Males	Females	Males	Females	Males	Females
0	0 (DW)	0	0	0	0	600	600	1.50	1.75	1.75	2.00	0.75	3.75
0	0 (CMC)-	0	0	0	0	600	600	1.50	2.25	2.50	3.00	3.25	2.50
3.88	6.17	0	0	0	0	600	600	1.75	3.75	2.75	4.25	1.50	3.50
12.93	20.57	0	0	0	0	600	600	2.25	4.75	2.00	3.75	2.25	4.00
38.80	61.70	0	2	0	4	600	500	2.00	2.75	1.25	1.33	2.25	3.00
Cyclophosphamide*****													
25	25	0	0	0	0	124	200	-	-	30.75	66.50	-	-

*4 Animals/dose/time period, each given single indicated dose level.
**Clinical signs observed in the indicated number of animals 24 to 48 hr after dosing included the following: ataxia, dyspnea, oral exudate.

***50 Metaphases per test-dose animal; 3 time groups/dose level (6, 24 and 48 hr after dosing).

****Derived by reviewer from Tables 8-19 of the Report to include gaps, chromatid breaks, rings, deletions, fragments, dicentrics, exchanges, and multiple damage.

*****Positive control sampled only 24 hr after dosing.

II. IN VIVO CYTOGENETICS STUDY IN RATS

(COMPOUND SX-1397, NALED TECHNICAL)

Report No. MRI-2-193-CCC-82-82

Date Started: 3 November 1982

Date Completed: 6 June 1983

Naled

Page _____ is not included in this copy.

Pages 33 through 39 are not included in this copy.

The material not included contains the following type of information:

_____ Identity of product inert ingredients.

_____ Identity of product inert impurities.

_____ Description of the product manufacturing process.

_____ Description of product quality control procedures.

_____ Identity of the source of product ingredients.

_____ Sales or other commercial/financial information.

_____ A draft product label.

_____ The product confidential statement of formula.

_____ Information about a pending registration action

X FIFRA registration data.

_____ The document is a duplicate of page(s) _____

_____ The document is not responsive to the request.

The information not included is generally considered confidential by product registrants. If you have any questions, please contact the individual who prepared the response to your request.

#5

004170

TOXICOLOGY BRANCH: DATA REVIEW

ICAL: NALED

Caswell No.: 586
EPA Chem. No.: 034401

TYPE: Teratology in rats

ION: Addendum to Teratology Study in Rats with Naled Technical (SX-1397); Project No. 583008; Chevron No. S-2276; Dosage Formulation Analyses

SION No./MRID No.: 253453/NA

OR/TESTING Lab.: Chevron Chemical (Ortho), Richmond, CA/ Science Applications Inc.

No./DATE: 721.11/S-2276/August 30, 1983

MATERIAL: Naled technical (SX-1397), 92.6% a.i.

DURES: Samples of the dosage formulations employed in a ratology study were analyzed by Chevron (see Attachment ERIMENTAL PROCEDURES, to this Review).

TS AND CONCLUSIONS: The analytical results were reported ven in Attachment II to this Review, indicating actual rdance of from approximately 85% to 100% of nominal ntrations at the three formulation dose levels, which is table to Toxicology Branch.

ALUATION/CORE: This study has already been reviewed by logy Branch under Acc.#252451 (Memo, May 22, 1984: to Miller) and adjudged CORE MINIMUM Data.

40

Naled

Page _____ is not included in this copy.

Pages _41_ through _54_ are not included in this copy.

The material not included contains the following type of information:

_____ Identity of product inert ingredients.

_____ Identity of product inert impurities.

_____ Description of the product manufacturing process.

_____ Description of product quality control procedures.

_____ Identity of the source of product ingredients.

_____ Sales or other commercial/financial information.

_____ A draft product label.

_____ The product confidential statement of formula.

_____ Information about a pending registration action

__X__ FIFRA registration data.

_____ The document is a duplicate of page(s) _____

_____ The document is not responsive to the request.

The information not included is generally considered confidential by product registrants. If you have any questions, please contact the individual who prepared the response to your request.